
Specialized mouse embryonic stem cells for studying vascular development.

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Public Summary:

Vascular progenitor cells are desirable in a variety of therapeutic strategies; however, the lineage commitment of endothelial and smooth muscle cell from a common progenitor is not well-understood. Here, we report the generation of the first dual reporter mouse embryonic stem cell (mESC) lines designed to facilitate the study of vascular endothelial and smooth muscle development in vitro. These mESC lines express green fluorescent protein (GFP) under the endothelial promoter, Tie-2, and Discomsoma sp. red fluorescent protein (RFP) under the promoter for alpha-smooth muscle actin (alpha-SMA). The lines were then characterized for morphology, marker expression, and pluripotency. The mESC colonies were found to exhibit dome-shaped morphology, alkaline phosphatase activity, as well as expression of Oct 3/4 and stage-specific embryonic antigen-1. The mESC colonies were also found to display normal karyotypes and are able to generate cells from all three germ layers, verifying pluripotency. Tissue staining confirmed the coexpression of VE (vascular endothelial)-cadherin with the Tie-2 GFP+ expression on endothelial structures and smooth muscle myosin heavy chain with the alpha-SMA RFP+ smooth muscle cells. Lastly, it was verified that the developing mESC do express Tie-2 GFP+ and alpha-SMA RFP+ cells during differentiation and that the GFP+ cells colocalize with the vascular-like structures surrounded by alpha-SMA-RFP cells. These dual reporter vascular-specific mESC permit visualization and cell tracking of individual endothelial and smooth muscle cells over time and in multiple dimensions, a powerful new tool for studying vascular development in real time.

Scientific Abstract:

Vascular progenitor cells are desirable in a variety of therapeutic strategies; however, the lineage commitment of endothelial and smooth muscle cell from a common progenitor is not well-understood. Here, we report the generation of the first dual reporter mouse embryonic stem cell (mESC) lines designed to facilitate the study of vascular endothelial and smooth muscle development in vitro. These mESC lines express green fluorescent protein (GFP) under the endothelial promoter, Tie-2, and Discomsoma sp. red fluorescent protein (RFP) under the promoter for alpha-smooth muscle actin (alpha-SMA). The lines were then characterized for morphology, marker expression, and pluripotency. The mESC colonies were found to exhibit dome-shaped morphology, alkaline phosphatase activity, as well as expression of Oct 3/4 and stage-specific embryonic antigen-1. The mESC colonies were also found to display normal karyotypes and are able to generate cells from all three germ layers, verifying pluripotency. Tissue staining confirmed the coexpression of VE (vascular endothelial)-cadherin with the Tie-2 GFP+ expression on endothelial structures and smooth muscle myosin heavy chain with the alpha-SMA RFP+ smooth muscle cells. Lastly, it was verified that the developing mESC do express Tie-2 GFP+ and alpha-SMA RFP+ cells during differentiation and that the GFP+ cells colocalize with the vascular-like structures surrounded by alpha-SMA-RFP cells. These dual reporter vascular-specific mESC permit visualization and cell tracking of individual endothelial and smooth muscle cells over time and in multiple dimensions, a powerful new tool for studying vascular development in real time.

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